Provisional Clinical and Surveillance Case Definitions for Guillain-Barré Syndrome

These provisional case definitions have been designed by group consensus* to be used for identification and case classification of reports of Guillain-Barré syndrome (GBS). They include both a case-finding surveillance case definition, and a clinical case definition for case categorization and classification. The case definitions are intended for use by public health and other medical personnel, and are designed to allow for stratification of certainty of a diagnosis of GBS in the setting of varying availability of clinical data. The Brighton Collaboration intends to develop definitive case definitions with guidelines for global use in the future. (www.brightoncollaboration.org/internet/en/index.html).

The **clinical case definitions** are stratified by levels of diagnostic certainty, moving from the case definition with the most supportive evidence for GBS (Level 1), to the case definition with less supportive evidence, but clinically consistent with a diagnosis of GBS (Level 3).

The **surveillance case definition** has been designed to assist in active case-finding; it is intended to be more sensitive, but, by necessity, less specific.

Footnotes are provided at the end of the document for clarification of certain aspects of the case definitions.

While these definitions have been designed to be used in the absence of additional consultation, persons using these case definitions are encouraged to consult with neurologists with expertise in neuromuscular medicine whenever possible, particularly when questions regarding interpretation of electrophysiologic results arise.

***GBS Case Definition Working Group Members**:*

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Clinical Case Definitions: Guillain-Barré syndrome (GBS)[1, 2]

Level 1 of diagnostic certainty: Guillain-Barré syndrome (in patients ≥2 years of age[3])

The *presence* of

- Subacute onset of flaccid weakness/paralysis, in limbs and/or cranial nerve-innervated muscles[4]

AND

- Bilateral onset of weakness/paralysis[5]

AND

- Decreased or absent deep tendon reflexes in affected limbs

AND

- Monophasic illness pattern, with subacute onset and progression followed by subsequent improvement, clinical plateauing, or death

AND

Presence of one of the following:

1. Electrophysiologic findings were abnormal and consistent with or suspicious for GBS, acute inflammatory demyelinating polyneuropathy (AIDP), or polyneuropathy[6]

OR

2. Histopathologic evidence of peripheral nerve demyelination or axonal degeneration by biopsy or autopsy

AND

An alternative diagnosis for weakness is not evident (see Table 1)[1]

Level 2 of diagnostic certainty: Guillain-Barré syndrome

(in patients ≥2 years of age[3])

The *presence* of

- Subacute onset of flaccid weakness/paralysis, in limbs and/or cranial nerve-innervated muscles[4]

AND

- Bilateral onset of weakness/paralysis[5]

AND

- Decreased or absent deep tendon reflexes in affected limbs

AND

- Monophasic illness pattern, with subacute onset and progression followed by subsequent improvement, clinical plateauing, or death

OR

- Presence of cytoalbuminologic dissociation (elevation of cerebrospinal protein >45 mg/dL, with absence of pleocytosis [CSF white cell count {total} <10 cells/mm^3])

AND

An alternative diagnosis for weakness is not evident (see Table 1) [1]

Level 3 of diagnostic certainty: Guillain-Barre syndrome (in patients ≥2 years of age[3])

The *presence* of

- Subacute onset of flaccid weakness/paralysis, in limbs and/or cranial nerve-innervated muscles[4]

AND

- Bilateral onset of weakness/paralysis[5]

AND

- Decreased or absent deep tendon reflexes in affected limbs

AND

An alternative diagnosis for weakness is not evident (see Table 1) [1]

Surveillance Case Definition[2]: Guillain-Barré syndrome

The *presence* of

- Subacute onset of bilateral flaccid weakness/paralysis, in limbs and/or cranial nerve-innervated muscles

Note: Level 1, 2, and 3 case definitions are enclosed for reference. These case definitions are intended to indicate levels of diagnostic certainty in the diagnosis of GBS, moving from most certain (Level 1) to least certain, but still likely (Level 3). These are provided as guides for interpretation of information that may accompany responses to the surveillance case definition.

Notes for Case Definitions

[1] If an **alternative diagnosis** explaining flaccid weakness/paralysis is present (Table 1), a diagnosis of Guillain-Barré syndrome is **excluded.** However, in many, if not most cases, a comprehensive documentation of testing for various other etiologies will either be incomplete or unavailable. These case definitions are provided to give guidance in the absence of detailed information on investigations for alternative etiologies of flaccid paralysis.

[2] It is recognized that there are several variants of polyneuropathy that are considered to be variants of Guillain-Barré syndrome that may not be captured under these case definitions. These include *Pure Sensory Neuropathy*, *Pure Autonomic Neuropathy*, and *Acute Inflammatory Polyradiculoneuropathy with Preservation of Stretch Reflexes*. However, these variants are very rare in the Western world, and the number of cases missed by these definitions due to the presence of these variants is considered to be extremely low.

[3] Levels of diagnostic certainty have been designed for adults and children older than or equal to 2 years of age. For children under the age of 2 years (and, in particular, those under the age of 6 months) the central and peripheral nervous system and, as such, the neurologic examination is continually in flux (e.g., what is "normal" in a 28-day old is not necessarily normal in a 2-month old child). The evaluation of polyneuropathy and neurologic deficits in infants and young children will need to be done in an age-appropriate fashion, taking into account the age and level of development of the child.

[4] Clinical nadir usually is reached by 4 weeks from onset of initial neurologic symptoms

[5] Weakness is usually, but not always, symmetric in nature, and usually has a pattern of progression from legs to arms. However, atypical patterns of progression may occur (e.g., beginning in the arms). Cranial nerve-innervated muscles may be involved, and may be present with or without the presence of limb weakness.

[6] Electrophysiologic patterns consistent with polyneuropathy
Interpretation should be documented or provided by a clinician with experience in assessing and interpreting electromyographic studies, and should be consistent with a demyelinating, axonal, or demyelinating / axonal peripheral neuropathy. In certain instances, electrophysiologic studies may be performed too early in the course of illness to allow for a clear demonstration of such changes; electrophysiologic findings that are interpreted as "abnormal", but not specified as being consistent with either GBS/polyneuropathy **or** a diagnosis other than GBS should ideally be discussed directly with a neurologist with electrophysiologic expertise.

Table 1: Exclusionary Criteria for a Diagnosis of Guillain-Barré syndrome

There are multiple other pathologic processes that may occur at various localizations in the central and peripheral nervous system that may present with a clinical picture similar to or identical to that of Guillain-Barré syndrome. If such a diagnosis explaining flaccid weakness/paralysis is present, this effectively excludes a diagnosis of Guillain-Barré syndrome, and the subject is considered "Not a case".

Examples of other diagnoses, grouped according to typically affected region, are provided below; this is not intended to be an exhaustive list, but rather to highlight the localizations within the nervous system that lesions or illness might occur, with examples provided:

- **Intracranial**
  carcinomatous meningitis

- **Spinal cord**
  infarct, myelitis, compression

- **Anterior horn cells of spinal cord**
  poliovirus and other RNA viruses causing poliomyelitis, including West Nile virus

- **Spinal nerve roots**
  chronic inflammatory demyelinating polyneuropathy

- **Peripheral nerves**
  metabolic derangements such as hypermagnesemia or hypophosphatemia
  tic paralysis
  snake bite
  heavy metal toxicity such as arsenic, gold and thallium.
  HIV infection
  porphyria
  critical illness neuropathy
  vasculitis

- **Neuromuscular junction**
  myasthenia gravis
  organophosphate poisoning
  botulism
  diphtheria

- **Muscle**
  critical illness myopathy
  polymyositis
  hypo/hyperkalemia